REMARKS

Claims 1-12 and 14 are canceled herein. New claims 16 and 17 are added which are directed to preferred embodiments of the invention relating to a method of whitening skin comprising orally administering compositions of the invention. Support for the new claims is found, for example, at page 8, line 18. No new matter is presented.

I. Information Disclosure Statement

Information Disclosure Statements were filed in this application on April 10, 2008 and April 21, 2008. Applicants respectfully request the Examiner to acknowledge receipt and return an initialed copy of the PTO/SB/08 Forms submitted therewith with the next Action.

II. Response to Claim Rejections under 35 U.S.C. § 103

A. Ancira

The Office Action indicates that claims 1-10, 12 and 14 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ancira et al (US PGPub 2004/0137077).

Claims 1-10, 12 and 14 are canceled herein, thereby rendering the rejection moot as to these claims. To the extent the rejection might be applied to present claims 16 and 17, Applicants provide the following.

In the Action dated February 21, 2008, the Examiner disagrees with Applicants assessment of the number of melanin inhibitors disclosed. The Examiner states that a review of the prior art reference discloses approximately 40 inhibitors and it is the Examiner's position that 40 would be considered a finite group of options and therefore, well within the skill and knowledge of the one of ordinary skill in the art to choose 2 from the disclosed list.

Further, the Examiner asserts that according to MPEP, it has been held that combinations of two or more compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is to be used for the very same purpose.

Applicants respectfully traverse the rejection.

First, Ancira discloses at least fifty total different melanin inhibitors and not forty as stated by the Examiner. It is not obvious for one of ordinary skill in the art to select a combination of tranexamic acid and L-cysteine (or a combination of tranxemic acid, L-cysteine, and ascorbic acid) among hundreds or thousands of possible combinations of more than 50 types of melanin inhibitors and it is not obvious to one skilled in the art that the particular claimed combination has excellent whitening effects and excellent effects to prevent pigmentation.

During an Interview on July 1, 2008, Applicants emphasized that it is not a matter of choosing two or three of the 50 listed melanin inhibitors, but whether one of ordinary skill in the art would have chosen the two claimed inhibitors in combination and that number of potential combinations of the fifty disclosed melanin inhibitors is in the hundreds, perhaps thousands, and may not be considered a finite number of possible solutions. Even if one of ordinary skill in the art were motivated to select two or three of the listed melanin inhibitors, there is no motivation to arrive at the specific combination of tranexamic acid and L-cysteine or tranexamic acid, L-cysteine and ascorbic acid as recited in the present claims.

However, the Examiner maintained that the listed group of 50 melanin inhibitors is a finite number of potential solutions such that it would have been obvious for one of ordinary skill in the art to try any of them to arrive at the present invention.

Applicants respectfully submit that the Examiner's interpretation of the reference as providing "a finite number" of options such that it would have been obvious for one of ordinary

skill in the art to try any of the listed melanin inhibitors in combination is legally incorrect. Specifically, in *Ortho McNeil Pharm. Inc. v. Mylan Labs, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008), the court states, "KSR posits a situation with a finite and in the context of the art, small or easily traversed, number of options." Also, in *Astrazeneca AB v. Mylan Labs, Inc. (In re Omeprazole Litigation)*, 490 F.Supp.2d. 381, 456 (S.D. N.Y 2007) it was stated that where there is no design need or market pressure, "thousands and thousands of permutations and paths" facing a person of ordinary skill in the art is not considered a finite number of options.

In this case, the Examiner has not identified a design need or market pressure and the potential number of combinations of the melanin inhibitors in the thousands is not a finite number of potential solutions. Thus, for at least this reason, a *prima facie* showing of obviousness has not been made.

Further, Ancira describes that its composition can be applied by means of "brush, dropper, atomizer, injector, sprayer, occlusive patch or pipette, etc." However, Ancira neither teaches nor suggests oral administration. Even if the melanin inhibitors described in Ancira have an effect via parenteral administration, it can not be said that same effect can be shown by oral administration. Accordingly, it is not obvious to one skilled in the art to determine, among hundreds or thousands of possible combinations of melanin inhibitors described (that are effective via parenteral administration), a specific combination having an effect via oral administration based on the disclosure of Ancira. For this additional reason, the present invention is not obvious over Ancira.

Further, it does not appear that the Examiner has considered the data provided in the specification and mentioned in the Response filed on August 13, 2007 since the Action does not address this point. Applicants reemphasize that although each of tranexamic acid, L-ascorbic

acid, L-cysteine, etc., may be known as an agent for preventing/treating pigmentations as a single agent (*cf.* the section of Background Art in the present specification), combinations of agents do not always exhibit excellent effects to prevent pigmentations. As a matter of fact, Table 1 of the present specification shows the following:

- L-ascorbic acid- and L-cysteine-administered group (sample (7)) did not exhibit a significant effect to inhibit pigmentations in comparison with the control (sample (I));

- L-ascorbic acid- and L-cysteine-administered group (sample (7)) did not exhibit an effect to inhibit pigmentations in comparison with L-ascorbic acid single administered group (sample (4)) and with L-cysteine single-administered group (sample (3)) and rather exhibited an effect to accelerate pigmentations; and

- Combination of tranexamic acid and L-cysteine (sample (6)) and combination of tranexamic acid, L-cysteine and L-ascorbic acid exhibited excellent effects to inhibit pigmentations. Combination of tranexamic acid and L-cysteine (sample (6)) and combination of tranexamic acid, L-cysteine and L-ascorbic acid (sample (8)) exhibited excellent effects to inhibit pigmentations.

This data shows that the combination of tranexamic acid and L-cysteine shows improvement over single administered ascorbic acid and single administered L-cysteine which was shown to accelerate pigmentations. That is, L-cysteine is shown to have the opposite desired effect when administered singly with ascorbic acid.

The excellent effects highlighted above and established in the specification were discovered for the first time by the present inventors in the present application and are

completely unexpected from the examiner's applied art. Therefore, for this additional reason, the present invention is patentable over Ancira.

Accordingly, Applicants respectfully request withdrawal of the §103 rejection based on Ancira.

B. Bundgaard et al

Claims 1-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bundgaard et al (U.S. Patent 5,073,641).

Claims 1-11 are canceled herein, thereby rendering the rejection moot as to theses claims. To the extent the rejection might be applied to present claims 16 and 17, Applicants submit the following.

According to the Examiner, Bundgaar discloses prodrugs of carboxylic acid agents which are capable of providing increased biomembrane transport so that the parent drugs are more bioavailable from the site of administration such as the gastro-intestinal tract, the rectum, the skin or the eye of the human body (column 3, lines 3-11). Bundgaar discloses the compounds disclosed include all diastereomers or enantiomers, or mixtures thereof (i.e. Examples of isomers are D-, L-, and DL-forms) column 5, lines 16-18). Non-toxic pharmaceutically acceptable acid salts may be included such as ascorbic acid (column 5, lines 20-29). Suitable drugs to inclusion into the formulation include tranexamic acid (column 9, line 39) and L-cysteine (column 9, line 60). While the specific compounds are disclosed in a list of compounds suitable for use, it is the position of the Examiner that the list constitutes a finite number of compounds and therefore, it

would have been obvious to a person of ordinary skill in the art to select two of the disclosed bio-effecting carboxylic acid agents disclosed.

The Examiner further states that it is generally considered to be *prima facie* obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose.

Applicants respectfully traverse the rejection.

The disclosure of Bundgaar is even less relevant than Ancira discussed above, since Bundgaar discloses even more compounds and thus thousands more potential combinations. Specifically, Bungaard neither teaches nor suggests a combination of tranexamic acid and L-cysteine (or a combination of tranxemic acid, L-cysteine, and ascorbic acid). Also, Bundgaard neither teaches nor suggests the whitening effect and the effect of inhibiting pigmentation or a method of whitening skin by oral administration. Accordingly, Bundgaard does not provide any motivation to reach the claimed composition of the present invention. Further the present invention provides unexpectedly superior effects as discussed above which would not have been expected based on the disclosure of Bundgaard.

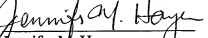
Accordingly, the present invention is not rendered obvious by Bundgaard and withdrawal of the rejection is respectfully requested.

III. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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